Pediatric Asthma—A Correlation of Clinical Treatment and Oxygen Saturation

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To determine the relationship between changes in room air oxygen saturation (SaO_2) and changes in the clinical signs of pediatric asthma patients after treatment with nebulized albuterol, a 9-month prospective observational study was conducted.

Eighty-two patients from 2 to 15 years of age who had exacerbations of asthma were studied when they presented to a military community hospital emergency department with an annual census of 62,500.

For each patient, the change in SaO_2 30 minutes after administration of nebulized albuterol was compared to the change in an ordinal clinical scoring system for asthma. Physicians were blinded to SaO_2 measurements. Data are reported as mean values with differences between groups analyzed using the paired t-test.

Patients with an initial SaO_2<95% who clinically improved after treatment had a mean increase in their SaO_2 of 2.6%. Patients with an initial SaO_2<95% who did not clinically improve after treatment had a mean decrease in SaO_2 of 1.1%, but this was not statistically significant (p=0.14). The positive predictive value for improved SaO_2 indicating clinical improvement is 98%. Patients with an initial SaO_2>95% did not have significant changes in SaO_2 after treatment regardless of clinical response.

For pediatric asthma patients with an initial SaO_2<95%, increased SaO_2 after treatment with inhaled albuterol is predictive of clinical improvement. Patients with an initial SaO_2<95% who do not have improved SaO_2 after treatment require further evaluation.

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Introduction

Several investigators have used various laboratory methods in an attempt to quantitate objectively the degree of respiratory distress of patients suffering from acute exacerbations of asthma. These studies have included measurements of FEV_1, peak-expiratory flow rates (PEFR),[1] and arterial blood gas concentrations (ABG).[2] Unfortunately, these laboratory studies are either effort-dependent or painful, and this makes their use with some patients, particularly small children, difficult if not impossible to perform.

Pulse oximetry noninvasively measures the percentage of hemoglobin bound to oxygen.[3] It has become an important tool in the evaluation of respiratory function of patients in the emergency department. For pediatric patients presenting with acute exacerbations of asthma, it can provide an objective means of evaluating a patient's degree of respiratory distress.

Some physicians use serial SaO_2 measurements during the treatment of acute exacerbations of asthma as a means of assessing the response to treatment.[4] However, different studies have reported both increasing and decreasing SaO_2 measurements in response to beta-2 agonists.[5-6] These contradictory data make the use of SaO_2 measurements to assess the response of asthmatics to albuterol a questionable practice.

The purpose of this study is to determine the relationship between changes in room air oxygen saturation (SaO_2) and changes in the clinical signs of pediatric asthma patients after treatment with inhaled albuterol.

Methods and Materials

All patients from 2 to 15 years of age who presented to the emergency department at Darnall Army Community Hospital with wheezing secondary to asthma were eligible for enrollment. Data were collected over a 9-month period. Exclusion criteria were: 1) the presence of lobar pneumonia, cardiovascular disease, foreign body aspiration, trauma, cystic fibrosis, or sepsis; or 2) severe respiratory compromise necessitating intubation before response to nebulized albuterol could be assessed. Mild respiratory infections consistent with a viral syndrome were not considered exclusionary. The study protocol was reviewed and approved by the hospital's institutional review board at Brooke Army Medical Center in San Antonio, Texas. Written informed consent was obtained from the legal guardians of study participants.

All of the patients who met our inclusion criteria had an initial SaO_2 measurement recorded by pulse oximetry (Physio-Control Lifestat 1600 Pulse Oximeter). The SaO_2 measurement recorded was the highest level observed over a 15 to 30-second period

accompanied by a correlating arterial pulse. The initial SaO_2 and all subsequent measurements were to be recorded by a nurse or medic. The physician treating the patient was blinded to these readings.

Prior to treatment each patient was examined by one of the emergency medicine residents or emergency department staff. During the initial examination the physician recorded the presence or absence of tachycardia, tachypnea, retractions, wheezing, or dyspnea. Each of these clinical signs was scored with the absence of the sign being given a score of 0, and the presence of the sign being given a score of 1 (Table 1). An overall score was generated by summing these 5 individual scores. Therefore, the patient could receive a maximum overall score of 5 (which would indicate severe symptoms) and a minimum overall score of 0 (which would indicate mild or no symptoms). Scores between 0 and 5 would indicate varying degrees of pulmonary compromise clinically observed in each patient before and after treatment. This scoring system has been used in past studies evaluating the severity of exacerbations of asthma.[7]

The patient was then given albuterol at a dosage of 0.15 mg/kg per treatment.[8] The albuterol solution was mixed with normal saline to a total of 3.5 cc to 4.0 cc. This was placed in either an Acorn II Nebulizer System or a face-mask nebulizer system (pediatric Aerosol Mask manufactured by Hudson Oxygen Therapy Sales Co) and powered by 100% oxygen at 6 L/min. The face mask system was used for younger patients who might not understand the proper use of a standard nebulizer system. The nebulizer treatments were given at approximately 20-minute intervals. Patients received up to 4 treatments or until their clinical findings had improved. At the discretion of the treating physician, patients could also receive oral or intravenous steroids during treatment in the emergency department. Prior to disposition, and at least 30 minutes after the last nebulizer treatment, the physician rescored the patient and a final SaO_2 was recorded. This time interval was used to ensure that the use of oxygen as a driving gas in the nebulizer would not affect our saturation measurements.

The mean and standard deviations for age, clinical score, and SaO_2 were calculated. The change in overall clinical score before and after treatment and the change in SaO_2 before and after treatment were analyzed using the paired t-test. The change in each clinical sign before and after treatment was analyzed by the McNemar test for correlate proportions. Effects with p-values of less than 0.05 were considered statistically significant. Standard measures of diagnostic accuracy (sensitivity, specificity, positive predictive value, negative predictive value) were calculated.

Table 1.—Clinical scoring system
Average respiratory rates and standard deviations.[12]

Clinical Parameter	Score=0	Score=1
Heart rate	> 120 beats/minute	> 120 beats/minute
Respiratory rate	> 2 standard deveations for age	> standard deviations for age
Dyspnea	Absent or mild	Moderate or severe
Accessory muscle use (retractions)	Absent or sub-costal retractions only	Intercostal and/or supraclavicular retractions
Wheezing	Absent or end expiratory only	Throughout expiration or expiratory and inspiratory

Results

Of the 82 patients entered in the study, 79 were treated by second-year or third-year emergency medicine residents or emergency department staff. The investigators (third year emergency medicine residents) treated 46 of the patients.

The mean age of the participants was 6.0+/-3.5 years. The overall score improved (ie, decreased) after treatment by a mean of 1.9+/-1.5 (Table 2). Of the 5 clinical signs scored, all improved after treatment except tachycardia (Table 3). The average SaO_2 for all patients improved (ie, increased) by 1.3+/-2.4% (Table 2).

The patients were then divided into 2 groups based on their initial SaO_2 on presentation. Patients with a pretreatment SaO_2<95% were placed in one group and those with a pretreatment SaO_2>95% were placed in the other group. Of the 54 patients whose pretreatment SaO_2<95%, 46 had an improvement in their overall score of at least 1.0 following treatment (Fig 1). The mean improvement in score for these 46 patients was 2.5+/-1.1 (Table 2). Again, all clinical signs in this group improved following treatment except tachycardia (Table 3). Of the 46 patients with an improved score, 40 showed improvement in their SaO_2 after treatment by at least 1.0% (Fig 1). The mean change in SaO_2 for all 46 patients was 2.6+/-2.1% (Table 2).

Eight patients with a pretreatment SaO_2<95% did not improve their clinical score following treatment (Fig 1). None of the clinical signs changed significantly after treatment (Table 2). As a group, the SaO_2 decreased by a mean of 1.1+/-1.9%, but this was not significant (P = 0.14) (Table 2). Of these 8 patients, only one had an improved SaO_2 after treatment (Fig 1).

For those patients with an initial SaO_2 <95%, the sensitivity and positive predictive value for improvement in SaO_2 after treatment reflecting clinical improvement were 87% and 98% respectively. The specificity and negative predictive value were 88% and 54%.

Of the 28 patients whose pretreatment SaO_2 >95%, 21 had an improved overall score after treatment (Fig 2). The mean increase was 2.3+/-1.1 (Table 2). All clinical signs improved after treatment except tachycardia (Table 3). There was no change in SaO_2. Seven patients with a pretreatment SaO_2 >95% had no improvement in their overall clinical score (Fig 2). None of the clinical signs changed significantly, and there was no change in SaO_2.

Discussion

Studies investigating changes in SaO_2 shortly after initiating treatment with inhaled bronchodilators found that SaO_2 initially decreases. Tal et al recorded SaO_2 before, during, and after treatment with inhaled albuterol and intravenous aminophylline in 18 patients from 3 months to 20 years of age with acute exacerbations of asthma. The SaO_2 initially decreased after beginning treatment and returned to pretreatment levels approximately 30 minutes after the initiation of therapy. No significant increases in SaO_2 were noted at any time after treatment regardless of whether the patient was admitted or discharged.[5] In 28 adults with asthma, Hedges et al noted similar changes in SaO_2 after inhaled metaproteranol.[9] Neither study compared the change in SaO_2 with changes in clinical signs.

The initial decrease in SaO_2 after treatment with inhaled beta-2 agonists is thought to be the result of increased ventilation/

perfusion mismatching in the lungs.[5,9] Because these medications initially stimulate vasodilation of the pulmonary vascular bed, there is increased perfusion of poorly ventilated areas of the lung which decreases SaO_2. Subsequent bronchodilation increases SaO_2 and alleviates the patient's respiratory distress. The overall effect on measured SaO_2 after treatment with inhaled beta-2 agonists is an initial decrease followed by an increase as bronchospasm is reversed. The time course for SaO_2 changes from beginning of the treatment to bronchodilation and increased SaO_2 is approximately 20 to 30 minutes.[5]

Studies that measured SaO_2 20 to 30 minutes after the initiation of therapy found no significant change from pretreatment levels regardless of clinical response.[5,7,10] In 200 children with asthma who were treated with inhaled albuterol, Karem et al compared the change in SaO_2 30 minutes after treatment between patients who were admitted and discharged. Discharged patients had no improvement in SaO_2 after treatment, while those who were admitted showed a small, insignificant increase. In 43 children less than 2 years of age with wheezing-related illnesses, Bentur et al compared the change in a clinical scoring system to the change in SaO_2 30 minutes after treatment. Although the clinical score improved following treatment, the SaO_2 did not change significantly.[10]

However, Yamamoto et al in looking at a large population of pediatric patients with wheezing found statistically significant increases in SaO2 following treatment with inhaled albuterol in patients whose pretreatment SaO_2 was low. Patients with higher pretreatment SaO_2 measurements did not show significant increases in SaO_2 after treatment.[6] Changes in SaO_2 were not compared to changes in clinical signs.

In our study, patients with an initial SaO_2 of <95% were placed into one group and those with an initial SaO_2 >95% into a second group. This division is based on the non-linear relationship between oxygen tension and SaO_2. Oxygen tension can be considered to reflect the degree of hypoxemia, and thus the severity of respiratory distress. At SaO_2 levels >95%, the oxyhemoglobin dissociation curve is flat, so oxygen tension (and thus clinical signs) may change dramatically with little change in the SaO_2. For SaO_2 levels <95%, the oxyhemoglobin dissociation curve is steeper, and changes in oxygen tension and clinical signs are reflected by changes in SaO_2.[11]

We compared the change in SaO_2 after treatment with the change in a clinical scoring system used in previous studies.[7,10] This scoring system is composed of 5 clinical signs associated with exacerbations of asthma. Assessment for the presence of these signs is not dependent on patient compliance and is easily accomplished at the bedside. The usefulness of this system in predicting the need to admit pediatric patients with asthma has been validated.[9] In our study, for patients who were judged to respond to treatment, there was improvement in all clinical signs except heart rate. The absence of change in heart rate is likely due to albuterol causing either a beta-2-stimulated vasodilation and reflex tachycardia or direct beta-1 stimulation of the heart.[5] Therefore, changes in heart rate should not be used in the assessment of clinical response to treatment with nebulized albuterol, and it should be removed from clinical scoring systems evaluating the response to beta-2 agonists in the future.

The results of this study show that for children with asthma who have an initial SaO_2<95%, improvement in SaO_2 after treatment with inhaled albuterol is a strong predictor of clinical improvement (PPV=98%). Although an increase in SaO_2 of 1% is accepted as significant, of the 40 patients with improved clinical signs and SaO_2 after treatment, 33 had an increase in SaO_2 of 2% or more (82.5%), and 24 had an increase in SaO_2 of 3% or more (60%) (Fig 3). Furthermore, it is important to recall that small increases in SaO_2 on the steep portion of the oxyhemoglobin dissociation curve represent significant increases in oxygen tension and relief of hypoxemia.

For patients with an initial SaO_2<95%, the negative predictive value for lack of improvement in SaO_2 after treatment indicating no clinical improvement is low (54%). Therefore, these patients require further evaluation to determine their medical needs. Of the 13 patients in our study with an initial SaO_2<95% who did not have an improvement in SaO_2 after treatment, the clinical response to treatment and eventually disposition of these patients varied considerably. Five patients showed considerable deterioration in their clinical scores and were admitted. Eight patients were discharged home, but only 5 had improvements in their clinical scores.

Regardless of the clinical response to inhaled albuterol, patients with initial SaO_2>95% did not have significant changes in SaO_2. Lack of improved SaO_2 after treatment with inhaled

Table 2.—Clinical scores and SaO_2 before and after treatment, as well as change in clinical score and SaO_2 with calculated p-values after treatment.

	No.	Age	Before Treatment Score	Before Treatment SaO_2	After Treatment Score	After Treatment SaO_2	Change in score	P-value of Change in Score	Change in SaO_2	P-value of Change in SaO_2
All Patients	82	6.0 +/- 3.5	3.1 +/- 1.6	94.7 +/- 2.3	1.2 +/- 1.4	96.0 +/- 2.4	1.9 +/- 1.5	<.0001	1.3 +/- 2.4	<.0001
Initial SaO_2≤95% and Clinical Improvement	46	5.9 +/- 3.2	3.7 +/- 1.3	93.4 +/- 1.8	1.2 +/- 1.1	96.0 +/- 2.1	2.5 +/- 1.1	<.0001	2.6 +/- 2.1	<.0001
Initial SaO_2≤95% and No Clinical Improvement	8	7.3 +/- 2.3	2.5 +/- 2.0	94.0 +/- 2.1	2.9 +/-2.3	92.9 +/- 3.6	-0.5 +/- 0.8	0.10	-1.1 +/-1.9	0.14
Initial $Sa0_1$>95% and Clinical Improvement	21	5.3 +/- 3.8	2.9 +/-1.4	97.0 +/- 0.9	0.5 +/- 0.6	97.1 +/- 1.7	2.3 +/- 1.1	<.0001	0.2 +/-1.7	0.61
Intital SaO_2>95% and No Clinical Improvement	7	7.0 +/- 4.5	1.3 +/- 1.8	97.4 +/- 1.0	1.4 +/- 1.8	96.7 +/-1.6	-0.1 +/-.0.4	0.36	-0.7 +/- 1.3	0.18

albuterol did not indicate lack of clinical response to treatment; therefore, changes in SaO_2 after treatment for this group of patients has little utility.

Conclusion

This study demonstrates that for pediatric asthma patients with an initial SaO_2<95%, increased SaO_2 after treatment with inhaled albuterol is predictive of clinical improvement. Failure to improve SaO_2 after treatment is not predictive of lack of clinical improvement, and further evaluation is required for appropriate disposition. In patients with an initial SaO_2>95%, changes in SaO_2 after treatment with inhaled albuterol are not indicative of clinical response. An understanding of the changes in SaO_2 in pediatric asthma patients following inhaled albuterol combined with appropriate clinical evaluation can facilitate the disposition of these patients.

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Fig 1.—Plot of change in score versus change in SaO_2 after treatment with inhaled albuterol for patients with intitial SaO_2≤95%.

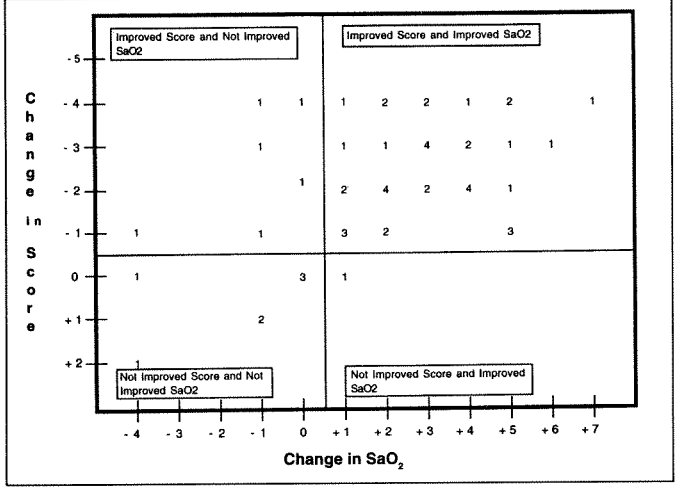

Fig 2.—Plot of change in score versus change in SaO_2 after treatment with inhaled albuterol for patients with initial SaO_2≤95%.

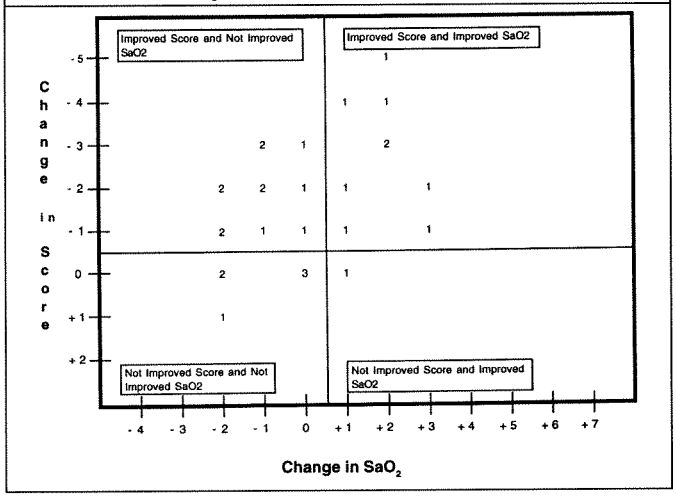

Table 3.—Percentage Change and Calculated p-values of Clinical Signs after Treatment with Inhaled Albuterol.

	No.	Change in HR	P-value of Change in HR	Change in RR	P-value of Change in RR	Change in DYS	P-value of Change in DYS	Change in RET	P-value of Change in RET	Change in WZ	P-value of Change in WZ
All Patients	82	+1%	1.00	-37%	<.0001	-44%	<.0001	-49%	<.0001	-67%	<.0001
Initial SAO_2≤95% and Clinical Improvement	46	-5%	0.75	-51%	<.0001	-54%	<.0001	-69%	<.0001	-80%	<.0001
Initial SaO_2≤95% and No Clinical Improvement	8	+58%	0.06	-13%	1.00	+12%	1.00	0%	1.00	-25%	0.50
Initial SaO_2>95% and Clinical Improvement	21	-9%	0.62	-52%	<.001	-57%	<.001	-38%	<.01	-76%	<.0001
Initial SaO_2>95% and No Clinical Improvement	7	0%	1.00	+15%	1.00	0%	1.00	0%	1.00	0%	1.00